HIV

Biological and demographic causes of high HIV and sexually transmitted disease prevalence in men who have sex with men

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Objectives: HIV disproportionately affects men who have sex with men (MSM). MSM and heterosexual networks are distinguished by biologically determined sexual role segregation among heterosexual individuals but not MSM, and anal/vaginal transmissibility differences. To identify how much these biological and demographic differences could explain persistent disparities in HIV/sexually transmitted disease prevalence in the United States, even were MSM and heterosexual individuals to report identical numbers of unprotected sexual partnerships per year.
Methods: A compartmental model parameterized using two population-based surveys. Role composition was varied between MSM and heterosexual subjects (insertive-only and receptive-only versus versatile individuals) and infectivity values.
Results: The absence of sexual role segregation in MSM and the differential anal/vaginal transmission probabilities led to considerable disparities in equilibrium prevalence. The US heterosexual population would only experience an epidemic comparable to MSM if the mean partner number of heterosexual individuals was increased several fold over that observed in population-based studies of either group. In order for MSM to eliminate the HIV epidemic, they would need to develop rates of unprotected sex lower than those currently exhibited by heterosexual individuals in the United States. In this model, for US heterosexual individuals to have a self-sustaining epidemic, they would need to adopt levels of unprotected sex higher than those currently exhibited by US MSM.
Conclusions: The persistence of disparities in HIV between heterosexual individuals and MSM in the United States cannot be explained solely by differences in risky sexual behavior between these two populations.

Over 20 years after HIV was identified in homosexual men, the US HIV epidemic continues to exact its greatest toll on men who have sex with men (MSM). In 2005, 51% of all new US HIV diagnoses occurred in MSM,[1] and an estimated 14–19% of urban US MSM are HIV positive.[2–4] Other sexually transmitted infections (STI) likewise affect MSM disproportionately.[5] The persistence of high HIV prevalence among MSM and low prevalence among US heterosexual individuals not reporting other risk factors (injection drug use, or contact with MSM or injection drug user) might be taken to imply vast differences in risky sexual behavior between the two groups. In the largest population-based survey of MSM to date,[2] however, the median number of unprotected anal sex partners per year among MSM was zero, with 75–85% of men reporting either zero or one unprotected anal intercourse (UAI) partner in the past year, a number comparable to that for heterosexual individuals (see supplementary material for derivation of these numbers, http://sti.bmj.com/supplemental). At the same time, at least two factors inherently distinguish MSM and heterosexual epidemics, regardless of relative partner numbers. First, heterosexual individuals are a two-sex population and MSM are one sex. As a result of this fundamental demographic difference, heterosexual individuals are necessarily ''role-segregated'' (men always insertive and women receptive) for sexual acts with high transmission probabilities (vaginal and anal sex), whereas MSM can be versatile. Previous work has demonstrated that role segregation can have a strong dampening effect on the efficient transmission of HIV through a population when there are differences in transmissibility for insertive and receptive roles.[6 7] Second, the predominant form of high-risk heterosexual contact (penile–vaginal sex) has a lower risk of transmission than the predominant form of high-risk MSM contact (penile–anal sex). We developed a mathematical model to assess the extent to which observed disparities in HIV morbidity between heterosexual individuals and MSM might be explained by these two biodemographic differences, factors independent of behaviors such as numbers of sex partners. We structured this as a ''thought experiment'' to identify how different MSM and heterosexual HIV epidemics in the United States would be if each population had the same patterns of sexual partnering.

METHODS

We developed a deterministic compartmental model to examine disease transmission dynamics, parameterized using data from two large population-based surveys of sexual behavior, the Urban Men's Health Study (UMHS)[2 8] and the National Health and Social Life Survey (NHSLS).[9] The model's structure and parameter values are explained in full in the supplementary material; here we outline the basic logic. The supplementary material and tables can be viewed on the *Sexually Transmitted Infections* website (http://sti.bmj.com/supplemental).

For heterosexual individuals, the population comprises eight compartments: two activity classes (high partner number, low partner number) crossed with two sexes (male, female) and two serostatuses (negative, positive). For MSM, the two sexes are replaced with three role classes (insertive-only, receptive-only, versatile). For both populations, there is an additional implicit compartment for individuals who never engage in unprotected anal or vaginal sex; their sole contribution is in forming the correct denominators. Population size is kept

Abbreviations: MSM, Men who have sex with men; NHSLS, National Health and Social Life Survey; STI, sexually transmitted infection; UAI, unprotected anal intercourse; UMHS, Urban Men's Health Study; UVI, unprotected vaginal intercourse constant for convenience. The initial population contains one seropositive, a highly active versatile (for MSM), and a highly active man (for heterosexual individuals).

For MSM, mixing among versatiles and non-versatiles is random in the sense that each partnering not involving two insertives or two receptives is equally likely, conditional on activity levels. This implies that versatiles have more partners than non-versatiles because they have more potential partners, a pattern seen in UMHS (supplementary table 1, see http://sti.bmj.com/supplemental).

HIV transmission probability estimates for unprotected anal and vaginal sex were taken from a published meta-analysis.[10] The number of sex acts, and thus per-partnership infectivity, varies depending on partnership composition (two low-activity individuals, two high-activity, or one of each; supplementary table 2, see http://sti.bmj.com/supplemental).

A common feature of sexual networks is activity-level homophily, the tendency for individuals to choose partners with similar sexual activity levels as themselves. We modeled this using an odds ratio approach rather than other approaches seen in the literature, because this automatically adjusts for changing population composition resulting from differential infection. Although this method has a clearer underlying relationship to statistical demography, it results in a model specification that can only be solved using numerical methods, which we implemented using Mathematica 5.0 (Wolfram Research, Inc., Champaign, Illinois, USA).

The parameter values used in each model are listed in table 1; their relationship to the source data and their derivations are described more fully in the supplementary material, which can be viewed at http://sti.bmj.com/supplemental.

RESULTS

We first consider scenarios in which both populations exhibit partnering levels similar to those reported by MSM. The baseline run (scenario 1) models an all-versatile MSM population with UAI infectivity levels. The prevalence trajectory for this population is shown in fig 1; model inputs and outputs are summarized in table 1. Scenario 2 portrays the MSM if all men were role-segregated (half taking each role); prevalence moves to less than half that of the comparable all-versatile population (equilibrium prevalence 9% instead of 19%). The area between scenarios 1 and 2 represents possible scenarios over which MSM can range based only on changes in versatility; scenario 3 shows MSM with a UMHS-derived versatility level, yielding 13% equilibrium prevalence.

The two-sex, role-segregated nature of heterosexual individuals suggests that if they had the same patterns of partnering as MSM, and engaged in UAI rather than unprotected vaginal intercourse (UVI), their epidemic trajectory would appear at the bottom of the range shown for MSM (i.e. scenario 2). By engaging in UVI instead of UAI (but with the same partnering rates), they would fall below the reproductive threshold, the level below which an epidemic dies out (scenario 4).

Another way to consider the differences between MSM and heterosexual individuals is to ask the question: how many partners would heterosexual individuals need in order to develop the same epidemic that MSM do in scenario 3 (observed levels of sexual role segregation)? Fixing the fraction in each activity class and the ratio of partner number for high and low-activity individuals, we find that achieving the same equilibrium prevalence as MSM requires heterosexual individuals to average 4.9 UVI partners annually, 2.7 times more partners than MSM (table 1, scenario 5). Following the same method, we see that at the reproductive threshold (the

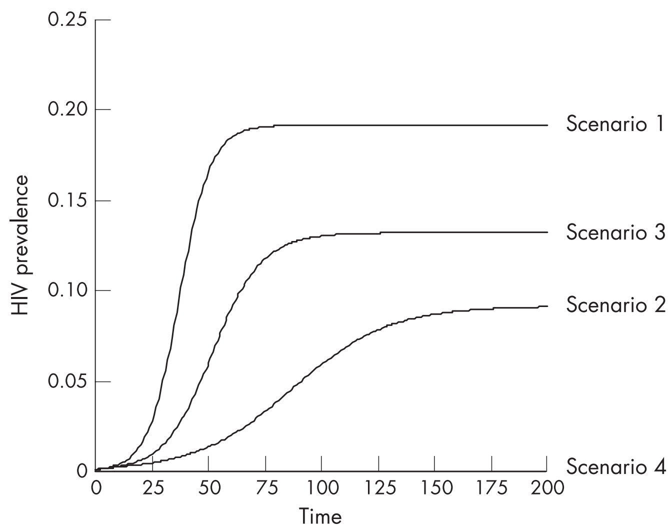


Figure 1 HIV prevalence over time with levels of partnering derived from reports of men who have sex with men (see text for details of scenarios).

Table 1 Simulation results

	Main source of parameters	UMHS (MSM)					NHSLS (heterosexual)	
	Scenario number	1	2	3	4	5	6	7
Inputs	Population type	MSM	MSM	MSM	**Het.**	**Het.**	MSM	**Het.**
	Level of infectivity	Anal	Anal	Anal	**Vaginal**	**Vaginal**	Anal	**Vaginal**
	% Versatile	100	–	**50**	**–**	**–**	**50**	**–**
	% Insertive	–	**50**	**35**	**50**	**50**	**35**	**50**
	% Receptive	–	**50**	**15**	**50**	**50**	**15**	**50**
	% No activity	62.8	62.8	62.8	62.8	62.8	**22.6**	**22.6**
	% Low activity	15.5	15.5	15.5	15.5	15.5	**66.5**	**66.5**
	% high activity	21.7	21.7	21.7	21.7	21.7	**10.9**	**10.9**
	No. partners (low activity)	1.0	1.0	1.0	1.0	**2.7**	1.0	1.0
	No. partners (high activity)	7.7	7.7	7.7	7.7	**20.7**	**2.4**	**2.4**
	Mean no. partners	1.8	1.8	1.8	1.8	**4.9**	**0.9**	**0.9**
	No. acts (high–high partnership)	10	10	10	10	10	10	10
	No. acts (high–low partnership)	50	50	50	50	50	50	50
	No. acts (low–low partnership)	250	250	250	250	250	250	250
	Initial HIV prevalence	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Output	Endemic prevalence	19.2%	9.2%	13.2%	0.0%	13.2%	41.2%	4.5%*

Bold type identifies any input differing from scenario 1.
Het., heterosexual; MSM, men who have sex with men; NHSLS, National Health and Social Life Survey; UMHS, Urban Men's Health Study.
*Note that although endemic prevalence is 4.5% in this scenario, the epidemic takes over 200 years before beginning to take off, in contrast to all other scenarios; this population is essentially at the reproductive threshold.

boundary between an epidemic or lack thereof), the average number of unprotected sex partners is 1.06 for MSM and 2.94 for heterosexual individuals; heterosexual individuals also need approximately 2.8 as many partners as MSM do to generate any epidemic at all. To isolate the effects of role versatility and anal/vaginal differentials, we also considered the mean partner numbers for a heterosexual population with an epidemic the size of scenario 2; this equals 4.1. Anal/vaginal differences alone raise the number of partners heterosexual individuals need to match MSM from 1.8 to 4.1; versatility raises that number further to 4.9.

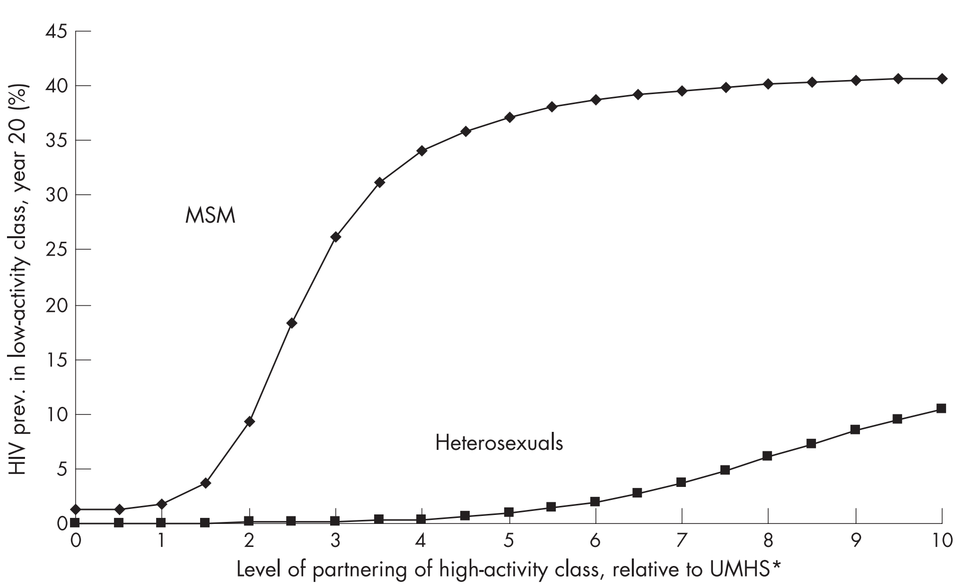
Other important differences reveal themselves when one considers not only endemic prevalence, but states of the epidemic at points in time before endemicity. We considered prevalence 20 years beyond the epidemic's introduction. One phenomenon that becomes clear at this time point is how low-activity heterosexual individuals and MSM (those with one unprotected sex partner per year) can be differentially affected by the activity of a minority of high-activity individuals. Under different levels of activity for the high-activity group, what is the level of HIV prevalence at year 20 for the low-activity group (whose behavior remains the same in all scenarios)? For scenario 3 (MSM with high-activity individuals having 7.7 partners per year), prevalence at year 20 for low-activity men is 1.7%, whereas for heterosexual individuals it is essentially zero. If the high-activity class doubled their partner numbers (presumably more in line with the sexual behavior of MSM at the start of the epidemic), prevalence among the low-activity group (whose behavior has not changed, and who overwhelmingly choose each other as partners), would rise to 9.3% for MSM, whereas heterosexual individuals would still be below the reproductive threshold, and have essentially zero prevalence. Fig 2 graphs this trend for more scenarios. We see that within a certain transition zone, HIV outcomes for MSM with relatively low levels of unprotected sexual activity are highly dependent on the activity of high-risk men. The same is true for heterosexual individuals; however, for MSM that transition zone is right at and above where sexual behavior seems to be occurring according to UMHS, whereas for heterosexual individuals it is far above realistic levels. US MSM populations exist near a boundary where the activity of a relatively small group of men can profoundly affect the health of many others.

Finally, we considered what would happen if both populations displayed behavior reported by heterosexual individuals. The NHSLS does not report partnership numbers for UVI exclusively, but we can develop estimates of these numbers by integrating data from a number of questions and introducing some simple assumptions (see supplementary material for description, http://sti.bmj.com/supplemental). Scenarios 6–7 show what happens to MSM and heterosexual individuals, respectively, under the resulting behavioral estimates. Heterosexual individuals are essentially on the reproductive threshold, the epidemic neither takes off nor dies out, but remains close to initial prevalence (0.1%) for centuries before crossing a threshold and producing a small (4.5%) epidemic. In contrast, the MSM epidemic is considerably larger than under reported MSM behavior, given the large proportion of the population that has moved from no-risk to low-risk; MSM also reach endemic prevalence much more quickly than heterosexual individuals (~40 years versus ~900 years). Taking the additional exercises we conducted above for MSM-reported behaviors and repeating them for heterosexual-reported behavior yields qualitatively similar results.

DISCUSSION

Although mathematical models have been used to assess the influence of patterns of sexual mixing,[11–15] HIV natural history,[16] and behavior change, vaccination, and antiretroviral use[17–21] on the HIV epidemic in MSM, such models have not previously been used to assess why MSM in developed nations have been so severely and persistently affected by HIV compared with heterosexual individuals. We developed a mathematical model of HIV transmission to assess the extent to which observed disparities in HIV morbidity between these groups might be explained by biological and demographic factors inherent to the two groups.

According to our model, if a US MSM population and a US heterosexual population both engaged in partnership patterns as reported by MSM, but MSM practiced versatility and UAI whereas heterosexual individuals practiced UVI, the MSM population would have a major HIV epidemic and the heterosexual individuals would have none. The same is true if both populations engaged in partnership patterns as reported by US heterosexual individuals. In order for MSM to eliminate the HIV epidemic, they would need to develop rates of



*eg, 3 = a high-activity class partnering level 3 times that seen in UMHS (3 × 7.7 = 23.1 partners/year)

Figure 2 HIV prevalence at year 20 of the epidemic for low-activity individuals, under different assumptions about the behaviors of high-activity individuals.
MSM, Men who have sex with men; UMHS, Urban Men's Health Study.

unprotected sex lower than those currently exhibited by heterosexual individuals in the United States. In order for US heterosexual individuals to have a generalized epidemic, they would need to adopt levels of unprotected sex several times higher than those currently exhibited by MSM. The health status for low-risk MSM in particular is highly dependent on the behavior of high-risk MSM; small changes among high-risk men can place many more low-risk men in danger. This is despite the fact that in our model, low-activity individuals overwhelmingly choose other low-activity partners. These findings illustrate the strong synergistic effect of biological and demographic elements inherent in MSM sexual networks in predisposing this population to an HIV epidemic, and perhaps to STI generally.

Our results differ from those of some previous models, and several limitations affect our work. In contrast to other models of heterosexual HIV,[22–25] our base model did not generate a significant heterosexual epidemic. This partly reflects the fact that we modeled vaginal heterosexual sex as a self-contained risk network, excluding injection drug use, heterosexual anal sex, and the bridging role of bisexual individuals. Recent data suggest that most heterosexually acquired HIV cases in the United States can be directly linked to a sex partner who is either an injection drug user or an MSM, and these bridging relationships have been important in generating and sustaining heterosexual HIV epidemics in developed nations.[26] A previous model assessing the UK HIV epidemic suggested that sexual transmission alone is too low to sustain a strictly heterosexual epidemic there.[27] Future models that include transmission via injection drug use and from bisexual men to women would be useful. In their absence, our model should not be interpreted as having demonstrated the impossibility of a sustainable HIV epidemic among heterosexual individuals in the United States. Our purpose was to assess how biological and demographic factors distinguishing MSM and heterosexual networks contribute to observed HIV disparities, and therefore we do not believe that the absence of injection drug use and bisexuality in our model detracts from the central findings.

The difference in heterosexual HIV dynamics between our model and others may also reflect the fact that many models assume that transmission probabilities per-partnership do not differ with the numbers of partners of individuals. Based partly on UMHS data, we assumed that individuals with many partners have fewer sex acts with any one of them, yielding a comparatively low per-partnership transmission probability among the most sexually active individuals. The estimated HIV transmission probability associated with different sexual acts is not well-defined, and transmission probability estimates for vaginal intercourse derived from studies in sub-Saharan Africa have typically been higher than those reported in studies from developed nations.[28] Our model would have demonstrated a larger epidemic in heterosexual individuals and smaller disparities by sexual orientation had we used such estimates.

We used a deterministic mathematical modeling framework. Such models do not easily incorporate factors such as concurrent sexual partnerships or higher-level network characteristics (e.g. tendencies for/against partner's partners forming sexual connections among MSM) that may influence the timing and magnitude of STI epidemics. These factors have been proposed to play a major role in distinguishing heterosexual HIV epidemics globally,[14] and are also likely to create differences between MSM and heterosexual HIV epidemics in the United States. Future modelling studies that incorporate these factors may better explain HIV transmission dynamics and observed disparities in HIV by sexual orientation.

Finally, for the sake of our ''thought experiment'' we compared scenarios in which MSM and heterosexual individuals have the same numbers of sex partners and the same sexual mixing patterns. They do not. The mean number of sex partners is undoubtedly higher among MSM than among heterosexual individuals, and these differences were considerably greater in the late 1970s when HIV was introduced. In addition, new partnership formation typically continues until older ages among MSM,[29] and mixing patterns by sexual activity level may vary by sexual orientation. Although we acknowledge that these factors almost certainly contribute to the observed disparities in HIV between MSM and heterosexual individuals, our findings suggest that these behavioral factors are not the only explanation for the vulnerability of MSM to HIV, and may not be the dominant risk for this population as a whole. More widespread recognition of these facts should temper prejudicial stereotypes related to MSM and STI. From a public health perspective, our findings suggest that in the absence of an effective vaccine, the level of behavior change required to bring the HIV epidemic under control among US MSM is substantially greater than that for heterosexuals. This alone does not suggest new public health interventions for MSM, but does reinforce the importance of the existing ones, and emphasizes that they may represent successful efforts even if they do not appear as such when measured against benchmarks derived from other communities.

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